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LETTER TO THE EDITOR

WILEY

Serum *Aspergillus fumigatus*-specific IgG antibody decreases after antifungal treatment in chronic pulmonary aspergillosis patients

To the Editor

Chronic pulmonary aspergillosis (CPA) is an uncommon and problematic pulmonary disease that is known to complicate many other respiratory disorders.[1] For the treatment of CPA, a minimum of 4–6 months oral triazole therapy is recommended initially,[2] however, the optimal duration of therapy for CPA is still unknown. Trends of the disease during the antifungal therapy should be monitored. It is difficult to gauge patient improvement. Radiological follow-up may be a viable alternative for assessing the progress of CPA.[2,3] However, radiological changes are too slow to reflect the progression of disease and very little change is visible in several months on computed tomography (CT) scans. Quantitative serological *Aspergillus* IgG assay might be a potential tool for monitoring disease progression and therapeutic response, though no substantive data exists to support its use.[4] Researchers now want to know whether the antibody titres can decline with successful therapy, and if it can be an indicator of the treatment outcome.

In clinical practice, we found some patients showed dynamic decrease of *Aspergillus* IgG level after antifungal treatment, and remained negative for a long time after therapy. Here, we report a case in detail and the remaining cases are briefly described.

A 63-year-old Chinese male. The main symptoms were excess cough and sputum production with hemoptysis for 8 months. The patient's related medical history was pulmonary tuberculosis. Chest CT scan revealed several pulmonary cavities with paracavitary infiltrates, including pleural thickening in left upper lung. Galactomannan (GM) assay (positive: ≥ 0.5 for serum and ≥ 0.8 for bronchoalveolar lavage fluid (BALF); Bio-Rad, France) was negative both for serum (0.45) and BALF (0.66). The results of *Aspergillus fumigatus (A. fumigatus)*-specific IgG (positive: ≥ 60 AU/mL; intermediate: 50–60 AU/mL; negative: <50 AU/mL; Dynamiker, Tianjin, China) were positive (74.23 AU/mL). Percutaneous lung biopsy pathology showed chronic granulomatous inflammation. The patient was subsequently diagnosed as chronic cavitary pulmonary aspergillosis and prescribed oral voriconazole. *A. fumigatus*-specific IgG were assessed at the 3rd and 6th month from initial antifungal treatment. The results were both negative (46.12 and 43.35 AU/mL). His clinical symptoms were obviously relieved, and chest CT scans (Figure 2) were stable after six months' antifungal treatment, then, antifungal treatment was stopped. In the following 3rd and 6th months, the *A. fumigatus*-specific IgG were both negative (41.31 AU/mL and 48.85 AU/mL), and the clinical symptoms and lung lesions were both stable. In addition, one female (23 years old) and two male (53/22 years old) patients were diagnosed as simple aspergilloma whose IgG presented similar trends just as this case. The indication of stopping therapy in these cases was defined as symptomatic improvement with negative findings from the testing of mycological samples, with or without radiological improvement, after the completion of at least 6 months of antifungal therapy. Their *A. fumigatus*-specific

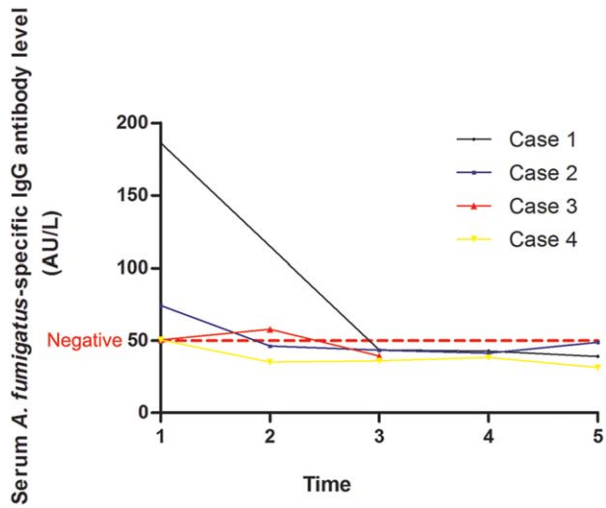

FIGURE 1 Dynamic changes of serum *Aspergillus fumigatus*-specific IgG antibody level. Time 1. All patients were positive for serum *Aspergillus fumigatus*-specific IgG antibody before antifungal treatment. Time 2. After 3 months of antifungal treatment, two out of 3 patients showed negative results and one patient remained intermediate (No data were collected from Patient 1 at the third month). Time 3. After 6 months of antifungal treatment, all patients showed negative results. Time 4, 5. At 3rd month and 6th month after therapy, all the specific IgG antibody remained negative. *, Case 2 in this figure was reported in detail in text

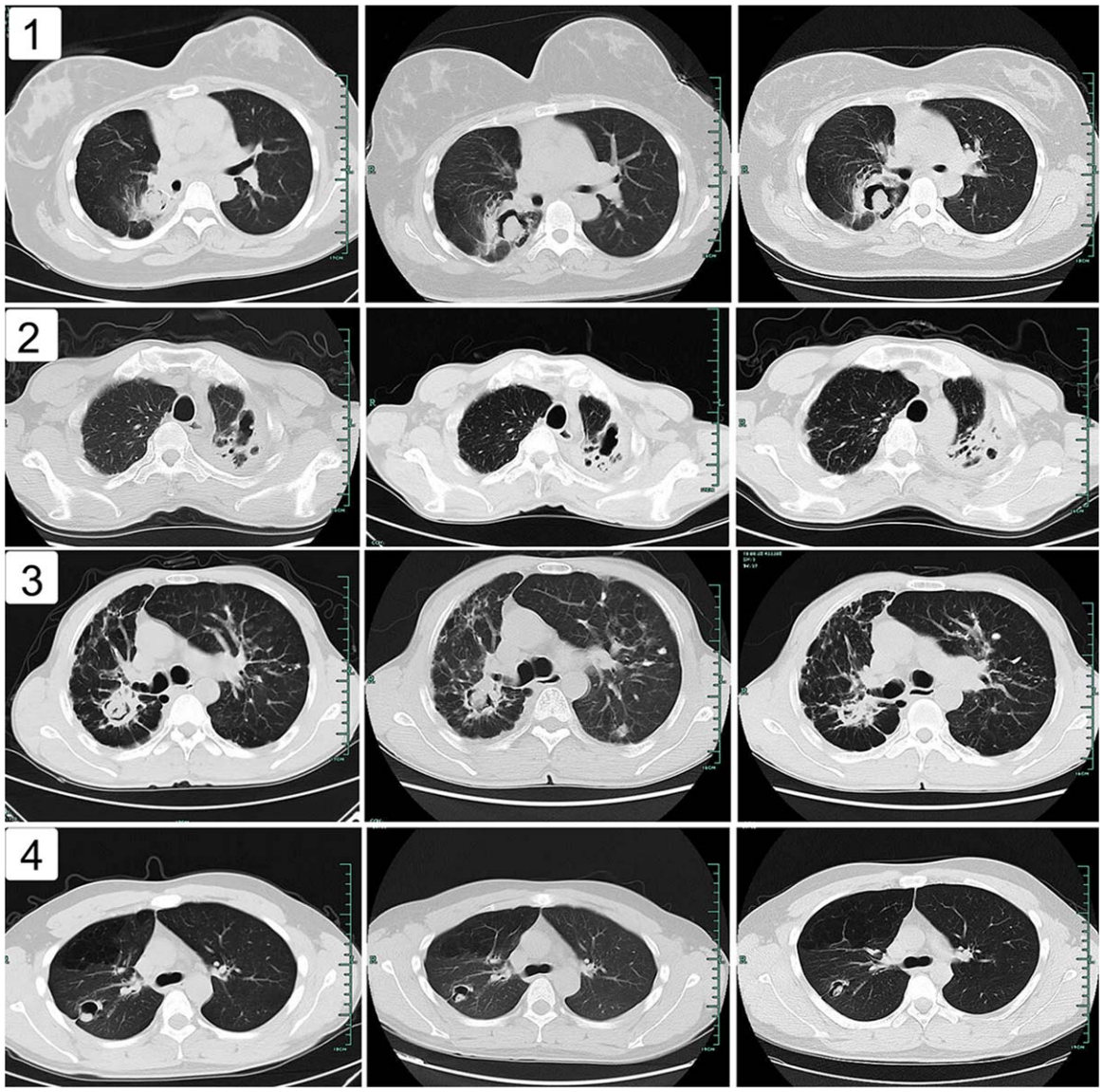

FIGURE 2 Chest CT images at the diagnosis, after antifungal treatment for six months and stopping antifungal treatment for six months. All the patients' chest CT scans showed a slight improvement after antifungal treatment for six months and were stable after stopping antifungal treatment for six months. *, Case 2 in this figure was reported in detail in text

IgG changes were showed in Figure 1 and chest CT imagines were showed in Figure 2.

The majority of CPA cases are predicted to occur as a complication of pulmonary tuberculosis, especially in resource poor countries where tuberculosis is common.[4] In China, tuberculosis is of high prevalence. Two out of 4 patients in our study had a pulmonary tuberculosis history. Raised *Aspergillus*-specific IgG antibody levels play a critical role in the diagnosis of CPA. Recently developed commercial ELISAs provide a promising alternative method that can be used for the serologic diagnosis of CPA. It has been reported that the sensitivity and specificity of commercial ELISAs range from 75% to 98% and 84% to 99%, respectively.[5] In this study, all patients presented raised IgG level, which confirms the clinical utility of IgG assay in CPA diagnosis. However, few studies have evaluated the clinical utility of serial monitoring *Aspergillus*-specific IgG levels to monitor disease progression and therapeutic response. Baxter et al. collected sera at two separate appointments within a 6-month period from 25 patients whom received antifungal therapy, to observe changing IgG levels over time. Unfortunately, the two assays used in their study (Platelia and ImmunoCap) did not show negative IgG levels after antifungal therapy, and there were no records of clinical features over the 6-month period.

Our findings demonstrated that *A. fumigatus*-specific IgG could fall to negative with effective antifungal therapy and remained negative in the following six months after stopping the treatment. In treatment monitoring of CPA, IgG assay has a lot of advantages compare with radiology such as

convenient access to serum samples, less radiation, reflecting instant disease condition and inexpensive. The exciting results might indicate that the *A. fumigatus*-specific IgG could be a useful biomarker to monitor the treatment efficiency and outcome of CPA.

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CONFLICT OF INTEREST

No potential financial conflict of interest exits in this study. No potential conflict of interest exists in the submission of this manuscript, and this manuscript is approved by all authors for publication.

AUTHOR CONTRIBUTIONS

Revised the manuscript: Yao
Performed research, analyzed data and wrote the paper: Zhou, Yao
Collected data: Yang, Lu
Played an important role in obtaining reagents: Yu
Contributed to supervision and designed research: Shen, Zhou

ETHICS

The study protocol was approved by The Institutional Review Board of Clinical Research of the First Affiliated Hospital, School of Medicine, Zhejiang University. All methods were performed in accordance with the approved guidelines and regulations and informed consent was obtained from all individual participants included in the study.

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